

```

=> "HCV core protein"
    10055 "HCV"
      19 "HCVS"
    10059 "HCV"
        ("HCV" OR "HCVS")
    294972 "CORE"
      63652 "CORES"
    326201 "CORE"
        ("CORE" OR "CORES")
    1821404 "PROTEIN"
    1271239 "PROTEINS"
    2118507 "PROTEIN"
        ("PROTEIN" OR "PROTEINS")
L36      521 "HCV CORE PROTEIN"
        ("HCV" (W) "CORE" (W) "PROTEIN")

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=> saponin
    15394 SAPONIN
    13771 SAPONINS
L37      19510 SAPONIN
        (SAPONIN OR SAPONINS)

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=> sterol
    23470 STEROL
    22729 STEROLS
L38      33903 STEROL
        (STEROL OR STEROLS)

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=> L37 and L38
L39      485 L37 AND L38

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=> L39 and L36
L40      0 L39 AND L36

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=> antigen and L39
    283704 ANTIGEN
    226601 ANTIGENS
    356550 ANTIGEN
        (ANTIGEN OR ANTIGENS)
L41      20 ANTIGEN AND L39

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=> HCV and L41
    10055 HCV
      19 HCVS
    10059 HCV
        (HCV OR HCVS)
L42      0 HCV AND L41

```

```

=> hepatitis and L41
    50747 HEPATITIS
L43      6 HEPATITIS AND L41

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=> D L43 IBIB ABS 1-6

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L43 ANSWER 1 OF 6 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2005:582493 CAPLUS
DOCUMENT NUMBER: 143:103237
TITLE: Synergistic adjuvants and antigens
        encapsulated into liposomes for prophylaxis and
        therapy
INVENTOR(S): Konur, Abdo; Graser, Andreas
PATENT ASSIGNEE(S): Vectron Therapeutics A.-G., Germany
SOURCE: Eur. Pat. Appl., 30 pp.
        CODEN: EPXXDW
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

```

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 1550458	A1	20050706	EP 2003-29801	20031223
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK				
WO 2005063288	A1	20050714	WO 2004-EP14630	20041222
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, VZ, VC, VN, YU, ZA, ZM, ZW				
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				

PRIORITY APPLN. INFO.:

EP 2003-29801 A 20031223

AB The present invention relates to liposome, mixts. or liposomes and liposomal compns. comprising at least two different adjuvants and a therapeutic agent, their production and use for the prevention and therapy of proliferative, infectious, vascular, rheumatoid, inflammatory, and immune diseases, in particular autoimmune diseases and allergies. Thus, antitumor effects of Pam3Cys and CpG-PTO ODNs as adjuvants were evaluated in mice inoculated with B16.F1 mouse melanoma cells. The tumor growth after immunization with low doses of antigenic peptide TRP-2 (SVYDFFVWL, 10 µg per animal) encapsulated in AVE3 liposomes (cholesterol/DLPE/DOPS), with or without 2.5 mol% Pam3Cys as liposomal adjuvant, combined with low doses CpG-PTO ODNs (1.3 nmol) in saline or encapsulated into AVE3 was compared. The tumor mass was reduced when mice were immunized with TRP-2 **antigen** encapsulated in AVE3, with or without 2.5 mol% Pam3Cys plus encapsulated CpG-PTO ODNs 17 days after B16 inoculation, demonstrating that the encapsulation of the CpG-PTO is necessary to achieve a partial tumor rejection. In addition, the application of two encapsulated adjuvants, Pam3Cys and CpG-PTO ODN, further improved antitumor effects, which is in accordance with the synergistic effects observed ex vivo. No significant increase of the survival rate could be achieved with AVE3/TRP-2 plus CpG-PTO in saline. When mice were immunized with AVE3/Pam3Cys/TRP-2 plus CpG-PTO in saline the mean survival time significantly increased to 16 days. When mice were immunized with AVE3/TRP-2, with or without Pam3Cys, plus liposomal CpG-PTO, the mean survival time significantly increased to 19 days. In addition, these data showed that incorporation of Pam3Cys into **antigen**-carrying AVE3 only significantly increases the survival time when the vaccine setting includes unencapsulated CpG-PTO.

REFERENCE COUNT: 7 THERE ARE 7 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L43 ANSWER 2 OF 6 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2005:563466 CAPLUS

DOCUMENT NUMBER: 143:103152

TITLE: Liposomal vaccine for the treatment of human hematological malignancies

INVENTOR(S): Mueller, Rolf; Graser, Andreas; Konur, Abdo; Mueller-Bruesselbach, Sabine

PATENT ASSIGNEE(S): Vectron Therapeutics Ag, Germany

SOURCE: Eur. Pat. Appl., 46 pp.

CODEN: EPXXDW

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 1547581	A1	20050629	EP 2003-29802	20031223
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK				

WO 2005063201 A2 20050714 WO 2004-EP14631 20041222
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH,
CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD,
GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC,
LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI,
NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY,
TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW,
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM,
AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK,
EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, MC, NL, PL, PT,
RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML,
MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.: EP 2003-29802 A 20031223

AB The present invention relates to liposomes and compns. comprising liposomes, their production and use for the prevention and therapy of proliferative diseases, infectious diseases, vascular diseases, rheumatoid diseases, inflammatory diseases, immune diseases, and allergies. Liposomes consisting of two neg. charged phospholipids (PS and PG) in combination with cholesterol can substitute liposomes consisting of cholesterol, PE and either PS or PG.

REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L43 ANSWER 3 OF 6 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2003:282425 CAPLUS

DOCUMENT NUMBER: 138:302637

TITLE: Intradermal vaccine compositions comprising **saponin**, **sterol**, and LPS derivative or CpG oligonucleotide as adjuvant

INVENTOR(S): Garcon, Nathalie

PATENT ASSIGNEE(S): Glaxosmithkline Biologicals S.A., Belg.

SOURCE: PCT Int. Appl., 27 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003028760	A2	20030410	WO 2002-EP10931	20020930
WO 2003028760	A3	20040311		
W:	AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW			
RW:	GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG			
CA 2461924	AA	20030410	CA 2002-2461924	20020930
EP 1432442	A2	20040630	EP 2002-777259	20020930
R:	AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, SK			
JP 2005507898	T2	20050324	JP 2003-532090	20020930

PRIORITY APPLN. INFO.: GB 2001-23580 A 20011001
WO 2002-EP10931 W 20020930

AB The present invention provides novel intradermal vaccines and novel uses for adjuvants in the preparation of intradermal vaccines, and also novel methods of treatment comprising them. The intradermal adjuvants, and methods, of the present invention comprise a **saponin** and a **sterol**, wherein the **saponin** and **sterol** are formulated in a liposome. The intradermal vaccine further comprises a LPS derivative or an immunostimulatory CpG oligonucleotide. The intradermal adjuvants are used in the manufacture of intradermal vaccines for humans, and in the intradermal treatment of humans.

ACCESSION NUMBER: 2000:116922 CAPLUS
 DOCUMENT NUMBER: 132:171114
 TITLE: Vaccine ISCOM adjuvant using **saponin** as sole detergent
 INVENTOR(S): Friede, Martin; Garcon, Nathalie
 PATENT ASSIGNEE(S): Smithkline Beecham Biologicals SA, Belg.
 SOURCE: PCT Int. Appl., 18 pp.
 CODEN: PIXXD2
 DOCUMENT TYPE: Patent
 LANGUAGE: English
 FAMILY ACC. NUM. COUNT: 1
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000007621	A2	20000217	WO 1999-EP5587	19990803
W: AU, CA, JP, US				
RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
CA 2339486	AA	20000217	CA 1999-2339486	19990803
AU 9955099	A1	20000228	AU 1999-55099	19990803
AU 738965	B2	20011004		
EP 1102600	A2	20010530	EP 1999-941506	19990803
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				
✓ JP 2002522397	T2	20020723	JP 2000-563304	19990803
✓ US 6506386	B1	20030114	US 2001-744800	20010604
PRIORITY APPLN. INFO.:			GB 1998-17052	A 19980805
			WO 1999-EP5587	W 19990803

AB The present invention provides an improved adjuvant formulation and a process for producing said adjuvant. The adjuvant comprises an ISCOM structure comprising a **saponin**, said ISCOM structure being devoid of addnl. detergent.

ACCESSION NUMBER: 1999:194018 CAPLUS
 DOCUMENT NUMBER: 130:227707
 TITLE: Vaccine adjuvant emulsions containing oils, **saponins**, and **sterols** and immunomodulators
 INVENTOR(S): Garcon, Nathalie; Momin, Patricia Marie Christine Aline Francoise
 PATENT ASSIGNEE(S): Smithkline Beecham Biologicals SA, Belg.
 SOURCE: PCT Int. Appl., 75 pp.
 CODEN: PIXXD2
 DOCUMENT TYPE: Patent
 LANGUAGE: English
 FAMILY ACC. NUM. COUNT: 1
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
✓ WO 9912565	A1	19990318	WO 1998-EP5714	19980902
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, GM, HR, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
CA 2302637	AA	19990318	CA 1998-2302637	19980902
AU 9896238	A1	19990329	AU 1998-96238	19980902
EP 1009430	A1	20000621	EP 1998-950005	19980902
R: BE, CH, DE, ES, FR, GB, IT, LI, NL				
JP 2001515870	T2	20010925	JP 2000-510462	19980902
US 6372227	B1	20020416	US 2000-486996	20000424
US 2002058047	A1	20020516		

PRIORITY APPLN. INFO.:

GB 1997-18901

A 19970905

WO 1998-EP5714

W 19980902

AB The present invention relates to an oil-in-water emulsion compns., their use in medicine, in particular to their use in augmenting immune responses to a wide range of **antigens**, and to methods of their manufacture The emulsion comprises a metabolizable oil, a **saponin**, and a **sterol**. For example, an emulsion was formulated containing squalene 5, α -tocopherol 5, Tween-80 2, and water to 100 %. An adjuvant contained 3D-MPL (immunomodulator) 50, QS21 50, the above emulsion 250, phosphate-buffered solution 250 μ L, and cholesterol 500 μ g.

REFERENCE COUNT: 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L43 ANSWER 6 OF 6 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 1998:239123 CAPLUS

DOCUMENT NUMBER: 128:307514

TITLE: Vaccines for infections and cancers

INVENTOR(S): Garcon, Nathalie; Friede, Martin

PATENT ASSIGNEE(S): Smithkline Beecham Biologicals SA, Belg.; Garcon, Nathalie; Friede, Martin

SOURCE: PCT Int. Appl., 31 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 2

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
✓ WO 9815287	A1	19980416	WO 1997-EP5578	19970930
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CB, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
CA 2267191	AA	19980416	CA 1997-2267191	19970930
AU 9747812	A1	19980505	AU 1997-47812	19970930
AU 714930	B2	20000113		
BR 9711853	A	19990824	BR 1997-11853	19970930
EP 939650	A1	19990908	EP 1997-910430	19970930
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, FI				
CN 1238696	A	19991215	CN 1997-180166	19970930
NZ 334734	A	20000526	NZ 1997-334734	19970930
JP 2001501640	T2	20010206	JP 1998-517196	19970930
ZA 9708868	A	19990406	ZA 1997-8868	19971003
NO 9901524	A	19990329	NO 1999-1524	19990329
KR 2000048866	A	20000725	KR 1999-702874	19990402
US 2001053365	A1	20011220	US 2001-819464	20010328

PRIORITY APPLN. INFO.:

GB 1996-20795

A 19961005

GB 1995-8326

A 19950425

EP 1996-910019

A 19960401

WO 1996-EP1464

W 19960401

WO 1997-EP5578

W 19970930

US 1997-945450

B2 19971212

US 1999-269383

W 19990402

AB The invention relates to a vaccine composition comprising an **antigen** and an adjuvant composition for treating infections or cancer. The adjuvant composition comprises alum, an immunol. active **saponin** fraction (e.g. QS21) associated with liposome containing a phospholipid and a **sterol** (e.g. cholesterol), and 3-de-O-acylated monophosphoryl lipid A. The **antigen** is derived from human immunodeficiency virus, feline immunodeficiency virus, varicella zoster virus, herpes simplex virus type 1 and 2, human cytomegalovirus, **hepatitis** A, B, C or E, respiratory syncytial virus, human papilloma virus, influenza virus, Hib, meningitis virus, Salmonella, Neisseria, Borrelia, Chlamydia, Bordetella,

Plasmodium, Toxoplasma, or cancer.
REFERENCE COUNT: 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS
RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

=> adjuvant and L36
31344 ADJUVANT
17168 ADJUVANTS
39289 ADJUVANT
(ADJUVANT OR ADJUVANTS)
L44 7 ADJUVANT AND L36

=> D L44 IBIB ABs 1-7

L44 ANSWER 1 OF 7 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2004:340992 CAPLUS
DOCUMENT NUMBER: 141:83504
TITLE: Enhancement of cellular immune response to DNA vaccine
encoding hepatitis C virus core and envelope 2 fusion
antigen by murine fms-like tyrosine kinase 3 ligand
AUTHOR(S): Ke, Jinshan; Zhao, Ping; Cao, Jie; Yu, Jiaping; Qi,
Zhongtian
CORPORATE SOURCE: Department of Microbiology, Second Military Medical
University, Shanghai, 200433, Peop. Rep. China
SOURCE: Shengwu Gongcheng Xuebao (2003), 19(2), 158-162
CODEN: SGXUED; ISSN: 1000-3061
PUBLISHER: Kexue Chubanshe
DOCUMENT TYPE: Journal
LANGUAGE: Chinese

AB Hepatitis C virus (HCV) is an important human pathogen that causes chronic liver disease worldwide. It is desirable to develop vaccines to prevent HCV infection, or at least to prevent progression to chronicity. An optimized hepatitis C virus core and envelope 2 fusion antigen DNA vaccine, which could induce humoral and cellular immune responses against HCV core and E2 protein in BALB/c mice efficiently, was constructed. Flt3 (Fms-like tyrosine kinase 3)-ligand (FL) was identified as an important cytokine for the generation of professional antigen-presenting cells, preferably dendritic cells. A DNA vaccine coexpressing the antigen and FL may activate immune responses more effectively. The influence of FL on this HCV DNA vaccine was evaluated. The cDNA encoding signal peptide and extracellular domain of murine FL was inserted into the plasmid pST-CE2t, and the resulting plasmid pST-CE2t/FL was transfected into COS7 cells. The HCV core and E2 protein were detected by Western blotting, and the soluble murine FL was detected by ELISA. Eight-week-old female BALB/c mice were inoculated i.m. with 100 µg pST-CE2t, pST-CE2t/FL, or mock vector, and boosted at the same dosage 3 w later. Anti-HCV core and E2 total IgG and isotypes were measured at w 1, 3, 5, 7. The splenocyte proliferative response to recombinant HCV core and E2 protein was detected at w 7. SF2/0 cells expressing **HCV core protein** were used as target cells for the detection of cytotoxic T lymphocyte (CTL) response. Western blot anal. showed that a protein band with mol. weight about 70 kD from lysate of COS7 cells transfected with plasmid pST-CE2t/FL could be detected by anti-HCV core or E2 monoclonal antibodies, which indicated that pST-CE2t could express glycosylated HCV core and E2 fusion protein. Murine FL could be detected in the culture supernatant of COS7 cells transfected with pST-CE2t/FL. Plasmid pST-CE2t immunized mice developed higher anti-HCV core and E2 IgG seroconversion rates and titers than pST-CE2t/FL group did at different various times, but the IgG2a/IgG1 ratio of anti-HCV E2 protein in pST-CE2t/FL group was much higher than pST-CE2t group. Splenocytes from pST-CE2t or pST-CE2t/FL immunized mice could proliferate with stimulation of HCV core or E2 protein in vitro, although pST-CE2t/FL group showed much stronger response. Splenocytes from mice immunized with pST-CE2t/FL induced 79.03% of target cell lysis at the effector/target ratio of 100:1 which was significantly greater than the lysis 62.2% observed in mice immunized with pST-CE2t. The data showed that the incorporation of FL can preferentially enhance the cellular response to this HCV fusion antigen DNA vaccine. And HCV specific antibodies were inhibited by FL in vaccinated mice, so, FL may be of potential value as an **adjuvant** in the development of DNA-based

immunization for prophylactic and therapeutic vaccine against HCV infection.

L44 ANSWER 2 OF 7 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2002:172843 CAPLUS

DOCUMENT NUMBER: 137:92307

TITLE: Additives and protein-DNA combinations modulate the humoral immune response elicited by a hepatitis C virus core-encoding plasmid in mice

AUTHOR(S): Alvarez-Lajonchere, Liz; Duenas-Carrera, Santiago; Vina, Ariel; Ramos, Thelvia; Pichardo, Dagmara; Morales, Juan

CORPORATE SOURCE: HCV Department, Centro Nacional de Genetica Medica, Havana City, Cuba

SOURCE: Memorias do Instituto Oswaldo Cruz (2002), 97(1), 95-99

CODEN: MIOCAS; ISSN: 0074-0276

PUBLISHER: Instituto Oswaldo Cruz

DOCUMENT TYPE: Journal

LANGUAGE: English

AB Humoral and cellular immune responses are currently induced against hepatitis C virus (HCV) core following vaccination with core-encoding plasmids. However, the anti-core antibody response is frequently weak or transient. In this paper, the authors evaluated the effect of different additives and DNA-protein combinations on the anti-core antibody response. BALB/c mice were i.m. injected with an expression plasmid (pIDKCo), encoding a C-terminal truncated variant of the **HCV core protein**, alone or combined with CaCl₂, PEG 6000, Freund's **adjuvant**, sonicated calf thymus DNA and a recombinant core protein (Co.120). Mixture of pIDKCo with PEG 6000 and Freund's **adjuvant** accelerated the development of the anti-core Ab response. Combination with PEG 6000 also induced a bias to IgG2a subclass predominance among anti-core antibodies. The kinetics, IgG2a/IgG1 ratio and epitope specificity of the anti-core antibody response elicited by Co.120 alone or combined with pIDKCo was different regarding that induced by the pIDKCo alone. Our data indicate that the antibody response induced following DNA immunization can be modified by formulation strategies.

REFERENCE COUNT: 22 THERE ARE 22 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L44 ANSWER 3 OF 7 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2002:128663 CAPLUS

DOCUMENT NUMBER: 137:92300

TITLE: Co-delivery of GM-CSF gene enhances the immune responses of hepatitis C viral core protein-expressing DNA vaccine: Role of dendritic cells

AUTHOR(S): Pu, Ou-Yang; Hwang, Lih-Hwa; Tao, Mi-Hua; Chiang, Bor-Luen; Chen, Ding-Shinn

CORPORATE SOURCE: Graduate Institute of Immunology, College of Medicine, National Taiwan University, Taipei, Taiwan

SOURCE: Journal of Medical Virology (2002), 66(3), 320-328

CODEN: JMVIDB; ISSN: 0146-6615

PUBLISHER: Wiley-Liss, Inc.

DOCUMENT TYPE: Journal

LANGUAGE: English

AB Hepatitis C virus (HCV) infection has become a critical public health problem worldwide. In Taiwan, it has been estimated that more than 300,000 people, 2% of the general population, have HCV infection. It has been well documented that direct delivery of gene i.m. can generate both humoral and cellular immunity, which more closely simulates the conditions of infection. In this study, female Balb/c mice immunized with HCV core plasmid DNA with or without **adjuvant** GM-CSF cytokine gene could induce both cellular immune response and HCV core-specific antibody titers after injection. Furthermore, the mice immunized with HCV core plus GM-CSF genes showed higher antibody titer and cytotoxic T cell activity compared to those of mice immunized with HCV core gene only ($P < 0.05$). To explore the effect of GM-CSF gene, the mice were immunized with reporter gene and cytokine gene plasmid. Increased levels of reporter protein and infiltrating cells around muscle tissue were noted. Moreover,

the protein could be detected in inguinal node 24 h after injection, especially in mice immunized with HCV/core plasmid plus GM-CSF gene. It was also observed that reporter protein expressing CD11c+ dendritic cells could be seen in the inguinal node. These data suggest that the GM-CSF gene did enhance HCV core specific immune response when coimmunized with HCV core DNA plasmid. Although more studies are needed, dendritic cells that appeared around the naked DNA injection area and that local lymph nodes might play a critical role in the immune response induced by naked DNA immunization.

REFERENCE COUNT: 39 THERE ARE 39 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L44 ANSWER 4 OF 7 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2001:467106 CAPLUS

DOCUMENT NUMBER: 136:182087

TITLE: A truncated **HCV core protein** elicits a potent immune response with a strong participation of cellular immunity components in mice

AUTHOR(S): Alvarez-Obregon, J. C.; Duenas-Carrera, S.; Valenzuela, C.; Grillo, J. M.

CORPORATE SOURCE: HCV Department, Vaccine Division, Centro de Ingenieria Genetica y Biotecnologia, Havana City, 10600, Cuba

SOURCE: Vaccine (2001), 19(28-29), 3940-3946

CODEN: VACCDE; ISSN: 0264-410X

PUBLISHER: Elsevier Science Ltd.

DOCUMENT TYPE: Journal

LANGUAGE: English

AB The immunogenicity of a truncated **HCV core protein** (Co.120) was studied in BALB/c and C57BL/6 mice, given three i.m. injections of antigen, adjuvanted with either aluminum hydroxide or Freund's **adjuvant**. A rapid antibody response was noted after the first dose, with both strains of mice eventually exhibiting comparable levels of anti-core IgG (titers >1:100000), with a mixed IgG1/IgG2a subclass response. Spleen cells from Co.120-immunized mice gave a significant specific proliferative response. IFN- γ gene expression was also detected after an ex-vivo specific stimulation of spleen cells in all immunized mice. This response was independent of dose, H-2 genetic background or type of **adjuvant**. The results indicated that immunization with the Co.120 protein elicits a potent anti-HCV humoral and cellular immune response.

REFERENCE COUNT: 38 THERE ARE 38 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L44 ANSWER 5 OF 7 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2000:337988 CAPLUS

DOCUMENT NUMBER: 133:280290

TITLE: Expression and immunological reactivity of recombinant **HCV-core protein**

AUTHOR(S): Dai, Wei; Ma, Weimin; Guo, Yabing

CORPORATE SOURCE: Shenzhen East Lake Hospital, Shenzhen, 518020, Peop. Rep. China

SOURCE: Zhonghua Ganzangbing Zazhi (2000), 8(1), 18-20

CODEN: ZGZZFE; ISSN: 1007-3418

PUBLISHER: Chongqing Yike Daxue, Dier Linchuang Xueyuan

DOCUMENT TYPE: Journal

LANGUAGE: Chinese

AB Objective. To express **HCV-core proteins** in E coli and to develop effective HCV core DNA-based vaccine. Methods. The vector that expresses the highly conserved HCV core genes were constructed. The pGEX-3X HCVCore constructs contained the 1-201 ncls (1-67aa, C201), 1-402 ncls (1-134aa, C402) and 1-591 ncls (1-197aa, C591), then expressed in E coli cells. Results. The products of HCV C201 and C402 genes were expressed as a fusion protein with glutathione-S-transferase (GST, 26kDa) whose mol. weight were 3.1x104 and 3.9x104 sep. C591 gene was not effectively expressed in E coli. The expressed proteins were sequestered within inclusion bodies (1B) and a variety of procedures designed to minimize 1B formation proved unsuccessful. The method finally adopted involved the purification of inclusion bodies followed by the

solubilization, purification, and refolding of the expressed protein. The purified C402 protein was antigenically reactive with serum from chronically infected HCV patients. BALB/C mice were immunized by a s.c. injection of C402 protein together with Freund's complete **adjuvant** which produced strong anti-HCV core humoral immune responses. Conclusion. It is important for the study of gene vaccine to construct a certain length of HCV core gene.

L44 ANSWER 6 OF 7 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 1996:42631 CAPLUS
DOCUMENT NUMBER: 124:84303
TITLE: High efficiency prokaryotic expression and purification of a portion of the hepatitis C core protein and analysis of the immune response to recombinant protein in BALB/c mice
AUTHOR(S): Hitomi, Y.; McDonnell, W. M.; Baker, J. R., Jr.; Askari, F. K.
CORPORATE SOURCE: Dep. Internal Medicine, Univ. Michigan, Ann Arbor, MI, 48109-0680, USA
SOURCE: Viral Immunology (1995), 8(2), 109-19
CODEN: VIIMET; ISSN: 0882-8245
PUBLISHER: Liebert
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Hepatitis C virus (HCV) produces chronic persistent liver infection in 1-2% of the U.S. population and is the leading cause of end stage liver disease in patients presenting for liver transplantation at our center. Efforts to cure persistent HCV infection are frequently unsuccessful, so the development of a HCV vaccine is a high priority. HCV envelope proteins are hypervariable so production of a recombinant surface antigen vaccine such as is available for hepatitis B is not likely to confer widespread, high level protective immunity. As the most highly conserved structural protein in the HCV genome, the core protein is one reasonable target for vaccine production. Presented here are data on the manufacture of recombinant core protein containing partial carboxy terminus deletions in an effort to increase the efficiency of core expression. The maltose binding protein (MBP) and glutathione S-transferase (GST) protein prokaryotic expression systems were used to study two different constructs, expressing the first 140 and 163 amino acids of the core region. Deletion of the 23 amino acids (aa) from aa141-163 led to a marked increase in the efficiency of protein production from <1 to 3-4 mg/L for both systems studied. Protein purification was accomplished using affinity chromatog. (MBP) or inclusion body isolation (GST) as determined by SDS-PAGE gels and immunotransblot with **HCV core protein**-specific monoclonal antibody. Finally, the immune response to recombinant protein was assessed in BALB/c mice using a MBP HCV core fusion protein and an ELISA developed using GST **HCV core protein** as a target. In all mice of this strain, serum anti-HCV core antibody titer increased to 10⁻⁴, two logs above background, following immunization in conjunction with Freund's complete **adjuvant**. These results represent an encouraging first step toward production of a core protein vaccine. Recombinant core protein is a useful tool to study the immune response to core protein and may be useful to further study the epidemiol. and biol. of the HCV virus.

L44 ANSWER 7 OF 7 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 1995:531308 CAPLUS
DOCUMENT NUMBER: 123:167108
TITLE: Hepatitis C virus core region: helper T cell epitopes recognized by BALB/c and C57BL/6 mice
AUTHOR(S): Kakimi, Kazuhiro; Kuribayashi, Kagemasa; Iwashiro, Michihiro; Masuda, Toru; Sakai, Masahiko; Ling, Wang; Kubo, Yoshinao; Kobayashi, Hirohiko; Higo, Kyoko; et al.
CORPORATE SOURCE: Institute Virus Research, Kyoto University, Kyoto, 606, Japan
SOURCE: Journal of General Virology (1995), 76(5), 1205-14
CODEN: JGVIAY; ISSN: 0022-1317
PUBLISHER: Society for General Microbiology
DOCUMENT TYPE: Journal

LANGUAGE: English

AB In this study, we characterized the B cell and T cell responses to the hydrophilic portion of hepatitis C virus (HCV) **core protein** in two strains of mice and identified the resp. antigen determinants. BALB/c (H-2d) and C57BL/6 (B6:H-2b) mice were immunized by a s.c. injection of recombinant **HCV core protein** together with Freund's complete **adjuvant**. The level of antibody production, as determined by ELISA, was consistently higher in BALB/c than in B6 mice. However, antibodies in sera from each strain bound to the N-terminal region of the core protein within amino acids 1 to 28 (MSTNPKPQRKIKRNTNRRPQDVKFPGGG), according to an experiment using non-over-lapping peptides that covered the hydrophilic portion of **HCV core protein**. The T cell responses were also higher in BALB/c than in B6 mice with respect to the proliferative responses of the draining lymph node cells in vitro. By limiting dilution cultures of the draining lymph node cells in vitro repetitively stimulated with recombinant core protein, T cell clones were established from both strains of mice and characterized. The surface markers of these clones were Thy-1.2+, CD3+, TCR $\alpha\beta$ +, CD4+ and CD8-. The proliferative responses were inhibited in the presence of anti-CD4 or anti-MHC class II monoclonal antibodies. The T cell lines in BALB/c mice recognized an epitope in HCV core at amino acids 72 to 91 (EGRAWAQPGYPWPLYGNEGL). The T cell lines in B6 mice recognized an epitope at amino acids 55 to 74 (RPQPRGRRQPIPKARQPEGR). Thus, mice with different MHC haplotypes recognized different non-overlapping T cell antigenic determinants of **HCV core proteins**.

ACCESSION NUMBER: 2001:50511 CAPLUS
 DOCUMENT NUMBER: 134:114821
 TITLE: Recombinant envelope vaccine against Flavivirus infection
 INVENTOR(S): Ivy, John; Bignami, Gary; Mcdonell, Michael; Clements, David E.; Collier, Beth-Ann G.
 PATENT ASSIGNEE(S): Hawaii Biotechnology Group, Inc., USA
 SOURCE: PCT Int. Appl., 44 pp.
 CODEN: PIXXD2
 DOCUMENT TYPE: Patent
 LANGUAGE: English
 FAMILY ACC. NUM. COUNT: 1
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001003729	A2	20010118	WO 2000-US18876	20000712
WO 2001003729	A3	20020912		
W:	AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM			
RW:	GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG			
US 6432411	B1	20020813	US 1999-352387	19990713
BR 2000013154	A	20020604	BR 2000-13154	20000712
PRIORITY APPLN. INFO.:			US 1999-352387	A 19990713
			WO 2000-US18876	W 20000712

AB A vaccine contains at least one Drosophila cell-secreted, recombinantly-produced form of a truncated Flavivirus envelope glycoprotein, as an active ingredient, and an adjuvant, as a critical component of the vaccine. The adjuvant is an immunomodulating agent having an iscom-like structure and comprising within the iscom-like structure at least one lipid and at least one **saponin**, and a pharmaceutically acceptable vehicle. Such a vaccine protects a subject against infection by a Flavivirus

ACCESSION NUMBER: 2002:128663 CAPLUS
DOCUMENT NUMBER: 137:92300
TITLE: Co-delivery of GM-CSF gene enhances the immune responses of hepatitis C viral core protein-expressing DNA vaccine: Role of dendritic cells
AUTHOR(S): Pu, Ou-Yang; Hwang, Lih-Hwa; Tao, Mi-Hua; Chiang, Bor-Luen; Chen, Ding-Shinn
CORPORATE SOURCE: Graduate Institute of Immunology, College of Medicine, National Taiwan University, Taipei, Taiwan
SOURCE: Journal of Medical Virology (2002), 66(3), 320-328
CODEN: JMVIDB; ISSN: 0146-6615
PUBLISHER: Wiley-Liss, Inc.
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Hepatitis C virus (HCV) infection has become a critical public health problem worldwide. In Taiwan, it has been estimated that more than 300,000 people, 2% of the general population, have HCV infection. It has been well documented that direct delivery of gene i.m. can generate both humoral and cellular immunity, which more closely simulates the conditions of infection. In this study, female Balb/c mice immunized with HCV core plasmid DNA with or without **adjuvant** GM-CSF cytokine gene could induce both cellular immune response and HCV core-specific antibody titers after injection. Furthermore, the mice immunized with HCV core plus GM-CSF genes showed higher antibody titer and cytotoxic T cell activity compared to those of mice immunized with HCV core gene only ($P < 0.05$). To explore the effect of GM-CSF gene, the mice were immunized with reporter gene and cytokine gene plasmid. Increased levels of reporter protein and infiltrating cells around muscle tissue were noted. Moreover, the protein could be detected in inguinal node 24 h after injection, especially in mice immunized with HCV/core plasmid plus GM-CSF gene. It was also observed that reporter protein expressing CD11c+ dendritic cells could be seen in the inguinal node. These data suggest that the GM-CSF gene did enhance HCV core specific immune response when coimmunized with HCV core DNA plasmid. Although more studies are needed, dendritic cells that appeared around the naked DNA injection area and that local lymph nodes might play a critical role in the immune response induced by naked DNA immunization.

REFERENCE COUNT: 39 THERE ARE 39 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

ACCESSION NUMBER: 1999:194018 CAPLUS
 DOCUMENT NUMBER: 130:227707
 TITLE: Vaccine adjuvant emulsions containing oils, **saponins**, and **sterols** and immunomodulators
 INVENTOR(S): Garcon, Nathalie; Momin, Patricia Marie Christine Aline Francoise
 PATENT ASSIGNEE(S): Smithkline Beecham Biologicals SA, Belg.
 SOURCE: PCT Int. Appl., 75 pp.
 CODEN: PIXXD2
 DOCUMENT TYPE: Patent
 LANGUAGE: English
 FAMILY ACC. NUM. COUNT: 1
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9912565	A1	19990318	WO 1998-EP5714	19980902
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, GM, HR, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
CA 2302637	AA	19990318	CA 1998-2302637	19980902
AU 9896238	A1	19990329	AU 1998-96238	19980902
EP 1009430	A1	20000621	EP 1998-950005	19980902
R: BE, CH, DE, ES, FR, GB, IT, LI, NL				
JP 2001515870	T2	20010925	JP 2000-510462	19980902
US 6372227	B1	20020416	US 2000-486996	20000424
US 2002058047	A1	20020516		

PRIORITY APPLN. INFO.: GB 1997-18901 A 19970905
 WO 1998-EP5714 W 19980902

AB The present invention relates to an oil-in-water emulsion compns., their use in medicine, in particular to their use in augmenting immune responses to a wide range of **antigens**, and to methods of their manufacture The emulsion comprises a metabolizable oil, a **saponin**, and a **sterol**. For example, an emulsion was formulated containing squalene 5, α -tocopherol 5, Tween-80 2, and water to 100 %. An adjuvant contained 3D-MPL (immunomodulator) 50, QS21 50, the above emulsion 250, phosphate-buffered solution 250 μ L, and cholesterol 500 μ g.

REFERENCE COUNT: 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

ACCESSION NUMBER: 1998:239123 CAPLUS
 DOCUMENT NUMBER: 128:307514
 TITLE: Vaccines for infections and cancers
 INVENTOR(S): Garcon, Nathalie; Friede, Martin
 PATENT ASSIGNEE(S): Smithkline Beecham Biologicals SA, Belg.; Garcon, Nathalie; Friede, Martin
 SOURCE: PCT Int. Appl., 31 pp.
 CODEN: PIXXD2
 DOCUMENT TYPE: Patent
 LANGUAGE: English
 FAMILY ACC. NUM. COUNT: 2
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9815287	A1	19980416	WO 1997-EP5578	19970930
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				

RW: GH, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, DE, DK, ES, FI, FR,
GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA,
GN, ML, MR, NE, SN, TD, TG

CA 2267191	AA	19980416	CA 1997-2267191	19970930
AU 9747812	A1	19980505	AU 1997-47812	19970930
AU 714930	B2	20000113		
BR 9711853	A	19990824	BR 1997-11853	19970930
EP 939650	A1	19990908	EP 1997-910430	19970930

R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,
IE, SI, FI

CN 1238696	A	19991215	CN 1997-180166	19970930
NZ 334734	A	20000526	NZ 1997-334734	19970930
JP 2001501640	T2	20010206	JP 1998-517196	19970930
ZA 9708868	A	19990406	ZA 1997-8868	19971003
NO 9901524	A	19990329	NO 1999-1524	19990329
KR 2000048866	A	20000725	KR 1999-702874	19990402
US 2001053365	A1	20011220	US 2001-819464	20010328

PRIORITY APPLN. INFO.:

GB 1996-20795	A	19961005
GB 1995-8326	A	19950425
EP 1996-910019	A	19960401
WO 1996-EP1464	W	19960401
WO 1997-EP5578	W	19970930
US 1997-945450	B2	19971212
US 1999-269383	W	19990402

AB The invention relates to a vaccine composition comprising an **antigen** and an adjuvant composition for treating infections or cancer. The adjuvant composition comprises alum, an immunol. active **saponin** fraction (e.g. QS21) associated with liposome containing a phospholipid and a **sterol** (e.g. cholesterol), and 3-de-O-acylated monophosphoryl lipid A. The **antigen** is derived from human immunodeficiency virus, feline immunodeficiency virus, varicella zoster virus, herpes simplex virus type 1 and 2, human cytomegalovirus, **hepatitis** A, B, C or E, respiratory syncytial virus, human papilloma virus, influenza virus, Hib, meningitis virus, Salmonella, Neisseria, Borrelia, Chlamydia, Bordetella, Plasmodium, Toxoplasma, or cancer.

REFERENCE COUNT: 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT